REMARKS

Status of the Claims

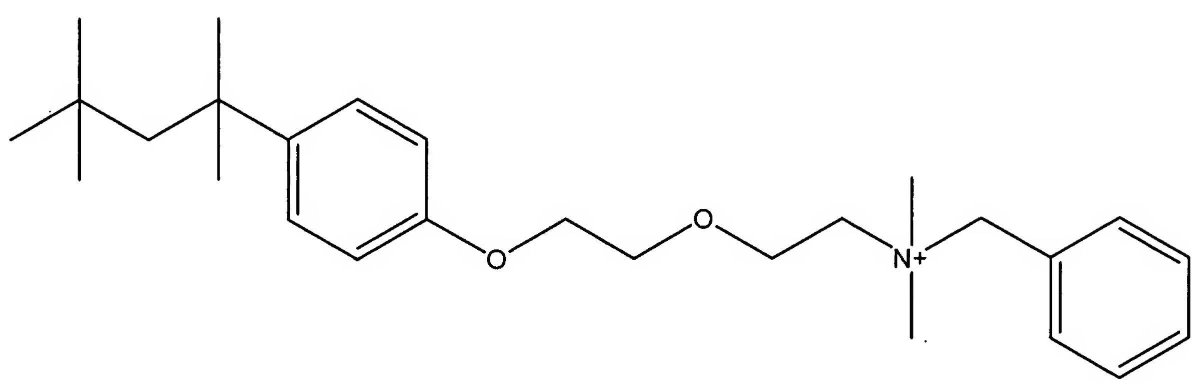
Claims 47-56 were previously pending. Claims 47-50 have been allowed. Claim 89 has been added, support for which can be found, for example, in Example 1. Accordingly claims 51-56 and 89 are at issue.

Rejections Under 35 U.S.C. §112, first paragraph

Claims 51 -56 stand rejected under 35 U.S.C. §112, first paragraph, for lack of enablement. The Examiner contends that while the specification is enabled for the benzethonium salt in the examples (i.e., benzethonium chloride), it is not enabled for formulations comprising any benzethonium salt. The Examiner further states that "[t]he predictability [sic: unpredictability] in this art is high since a small change . . . could result in a drastic change in activity . . ."

Applicants respectfully traverse this rejection and request reconsideration.

The term "benzethonium" denotes a specific quaternary ammonium ion, which is set forth below:



Consequently, the term "benzethonium salt" (which is recited in claim 51 as "a benzethonium salt" merely to provide correct antecedent basis) has only one variable component, i.e., the anion.

It is well-known in the art that the microbiocidal activity of quaternary ammonium compounds lies in the quaternary ammonium cation, not the anion. Ullman's Encyclopedia of Industrial Chemistry ("Ullman"), 5th Ed. (1990) (Exhibit A) characterizes the entire class of quaternary ammonium compounds as microbiocides:

> Quaternary ammonium compounds are most effective against gram-positive bacteria at concentrations as low as 1:200 000. ...

(Exhibit A, p. 566). Ullman does not disclose or suggest that only the chloride salts of quaternary ammonium compounds are microbiocidal. In fact, several non-chloride quaternary ammonium compounds have been shown to be anti-microbial. For example, the propionate salt of didecylmethylpoly(oxyethyl)ammonium is sold as a disinfectant (Exhibit B). See also, col. 3, lines 61-62, and col. 5, lines 45-61, of U.S. Patent No. 5,753,600 (disclosing that the anion of an antibacterial benzalkonium salt can be, for example, an amino acid, fatty acid, or an anionic residue of phosphate, phosphonate, sulfonate, or sulfate having an alkyl or alkenyl group of branched or straight chain 1-30 carbon atoms).

Furthermore, several issued U.S. patents refer to benzethonium salts generally as antimicrobial agents. See, for example, claim 3 and col. 3, lines 12-17, of U.S. Patent No. 6,790,460; claims 8, 27, 36, and 45 of U.S. Patent No. 6,057,015.

Additionally, a chloride anion alone is biocidally inactive up to rather high concentration (otherwise there would be no life in the ocean). Therefore, the activity of benzethonium chloride clearly resides in the benzethonium cation, not the chloride anion.

For the foregoing reasons, the claims are enabled for benzethonium salts generally. Accordingly, applicants respectfully request withdrawal of this rejection.

Applicants do not understand the last sentence in the first paragraph of page 3 of the Office Action, which states that "[t]he group of benzethonium salts created should be structurally similar to benzethonium salts." Applicants respectfully request clarification of this statement.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

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Respectfully submitted,

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Ullmann's Encyclopedia of Industrial Chemistry

Fifth, Completely Revised Edition

Volume A 16:
Magnetic Materials to Mutagenic Agents

Editors: Barbara Elvers, Stephen Hawkins, Gail Schulz

VCH

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Microbiocides

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The term microbiocide (or more simply biocide) is used to describe all agents that kill microbial life and thus includes antibiotics (→Antibiotics), antimicrobial agents used in medicine (→ Chemotherapeutics), disinfectants (→ Disinfectants), and agricultural fungicides (→ Fungicides, Agricultural). This article will, however, deal mainly with the compounds used to prevent microbial growth in industrial products, particularly in the food industry, in cosmetics, pharmaceuticals and toiletries, in paints and plastics, in water cooling systems, and in paper manufacture. The use of microbiocides in wood preservation is discussed elsewhere (→ Wood Preservation).

History. Chemicals have been used since the very earliest times in the prevention of disease and the preservation of food. Notable examples were the use of burning sulfur to control the spread of plague and the widespread use of spicing, salting, and smoking to prevent the deterioration of food. The use of chemicals in earlier times was quite empirical since nothing was known about the mechanisms by which they effected the preservation of food or the control of disease. However, these empirical observations were supplemented by a more rigorous scientific investigation following the discovery of the microscope by VAN LEEUWENOEK in the 18th century.

VAN LEEUWENOEK demonstrated the presence of major classes of bacteria, protozoa, algae, and yeasts. The causal relationship between microorganisms and disease was established by the research work of BASSI and PASTEUR on the infection of silk worms by fungi and protozoa, respectively. Major contributions were subsequently made by KOCH and LISTER in the isolation and identification of pure bacterial strains as pathogens responsible for disease. Recognition of the fact that bacteria are responsible for disease and food spoilage created much interest in the development of chemicals for the control of these bacteria. Methods developed by KOCH and others were used in evaluating the effectiveness of these chemicals in destroying bacteria and curing disease. In the latter half of the 19th century, LISTER demonstrated that the use of phenol markedly reduced the incidence of serious infection during surgery. LISTER's work demonstrated the potential of chemical disinfectants in hospitals; subsequently, the use of less toxic and more efficient chemicals was extended to other areas of hospital practice.

The preventative role of chemical biocides was also becoming recognized in the industrial field. The use of biocides in metal working fluids, for example, is an important factor in maintaining product quality and the health of the work force. In oil recovery, biocides are used to control sulfate-reducing bacteria and to improve yields. In water cooling systems and paper production, added biocides prevent the formation of bacterial or fungal slimes thus avoid-

1,3-Dichloro-5,5-dimethylhydantoin [*118-52-5*] is sparingly soluble in water with which it reacts to give controlled release of hypochlorous acid. 1-Bromo-3-chloro-5,5-dimethylhydantoin [*126-06-7*] reacts with water to form both hypochlorous and hypobromous acids. The latter has a wider pH range of bactericidal activity than hypochlorous acid. When hypobromous acid comes into contact with nitrogenous waste, bromamines are formed which, unlike the chlorine analogues, retain a significant biocidal activity.

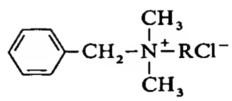
1.3. Iodine and Iodophores

Iodine [*7553-56-2*] has a wide range of antimicrobial activity and is effective against gram-positive and gram-negative bacteria, mycobacteria, fungi, and viruses. It also kills bacterial spores after an extended contact time. The active species (the iodine molecule) is only sparingly soluble in water; iodine is therefore used as a solution of iodine in alcoholic potassium iodide.

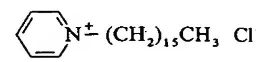
Iodine stains the skin and may lead to sensitization of the skin and mucous membranes. Iodophores (iodine carriers) were developed in the 1950s in order to overcome these disadvantages. Iodophores are essentially complexes of iodine with various organic compounds which release iodine on demand. The most important complexes used are those with poly(propylene oxide) or poly(ethylene oxide), cationic surfactants (quaternary ammonium salts), or polyvinylpyrrolidone. The iodophores are used in hospitals primarily for skin disinfection, and also in dairy farming where they are important as udder washes in the prevention of bovine mastitis as, for example, the Iosan range of iodophores (Ciba-Geigy, Switzerland) or Iodel FD (Diversey, UK).

1.4. Quaternary Ammonium Compounds

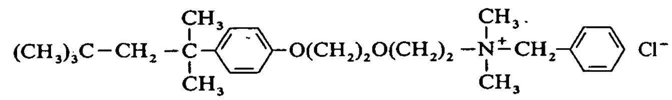
Quaternary ammonium compounds are most effective against gram-positive bacteria at concentrations as low as 1:200 000. They are less active against gram-negative organisms: concentrations as high as 1:20 000 are required to control *Pseudomonas aeruginosa*. Further limitations of quaternary ammonium compounds are their inactivity at and below pH 3.5 and their reduced effectiveness under dirty conditions. They are nontoxic and are used quite widely in hospitals, in the food industry, and as household disinfectants. Commercially important quaternary ammonium disinfectants are benzalkonium chloride [*8001-54-5*], benzethonium chloride [*121-54-0*], and cetylpyridinium chloride [*123-03-5*]:



Benzalkonium chloride



Cetylpyridinium chloride



Benzethonium chloride

Amphoteric quaternary ammonium disinfectants, usually alkylated aminocarboxylic acid derivatives, are also used commercially. The amphoterics have greater caustic stability than the normal quaternaries and are more easily removed from surfaces. This is a great advantage in the food industry where amphoterics are widely used. The formula of Tego 103 S (Goldschmidt, FRG) is given below:

$RNH(CH_2)_2NH \cdot (CH_2)_2NH \cdot CH_2 \cdot COOH \cdot HCl$

1.5. Biguanides

Although the biguanides had been recognized as biologically active by IG Farben in the 1930s, their potential as active bactericides was first discovered by ICI in 1946 [1], [2] in the form of the biguanide polymer, poly(hexamethylene biguanide) hydrochloride [*32289-58-0*] (PHMB). Subsequently, 1,6-bis(4′-chlorophenyl biguanide) hexane [*55-56-1*] (chlorhexidine) was also found to be a potent biocide. Chlorhexidine and PHMB, are the major biguanide compounds which are used today as disinfectants and sanitizers [3].

Chlorhexidine is bactericidal at concentrations of 100 µg/mL and bacteriostatic at concentrations of 1 µg/mL. It is often formulated with 2-propanol and quaternary ammonium compounds. It is absorbed by the skin and is widely used as a topical disinfectant in hospitals. It is sold under the trade name of Hibitane (ICI, UK).

Products by Groups

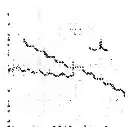
Product group Quaternary Ammonium Compounds

Description:
Our quaternary ammonium compounds are used as disinfectants, sanitizers, deodorants, fungicides and cationic surfactants in fomulations for household, institutional, industrial cleaners, water treatment, personal care and wood protection applications.

Product subgroup Dialkyl Quats

Description:
Dialkyl quats are a class of quaternary ammonium compounds generally used as disinfectants, sanitizers and algaecides. They are particularly effective against difficult to control organisms in hard water and in the presence of organic soil.

Product Bardap® 26



Product Name	Bardap® 26
Chemical Name	N,N-Didecyl-N-methylpoly(oxyethyl)ammoniumpropionate (in ca. 10%Ethylenglycol / ca. 18% Polyethylenglycol)
Synonyms	Didecylmethylpoly(oxethyl) Ammonium Propionate
Form	Liquid
Quality	Active ingredient (%): 70
Description	Bardap® 26 find uses in disinfectant for instruments and wood preservative due to its low corrosion properties.
Attributes	Globally sourced biocides are offered for applications and markets outside the US and Canada.
Contact	mailto:contact.allendale@lonza.com

Product search

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